

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 16 MAY 2006

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Applicant's or agent's file reference TX/4-33565A	FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/EP2005/000541	International filing date (day/month/year) 20.01.2005	Priority date (day/month/year) 21.01.2004	
International Patent Classification (IPC) or national classification and IPC INV. C07D209/42 A61K31/404			
Applicant NOVARTIS AG et al.			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 15.06.2005		Date of completion of this report 15.05.2006	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Kollmannsberger, M Telephone No. +49 89 2399-	



**INTERNATIONAL PRELIMINARY REPORT
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International application No.
PCT/EP2005/000541

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-15 as originally filed

Claims, Numbers

1-10 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1; 5-8 (part), 10

because:

☒ the said international application, or the said claims Nos. 10 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1; 5-8 (part) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or Industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2-4, 9; 5-8(part), 10(part)
	No: Claims	
Inventive step (IS)	Yes: Claims	2-4, 9; 5-8(part), 10(part)
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-9
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III

III-1. Present claims 1, 5-8 and 10 (insofar as they relate to subject-matter defined in claim 1) relate to compounds/methods defined by reference to a desirable characteristic or property, namely being selective agonists of the S1P4 receptor. The claims cover all compounds/methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds/methods. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope was impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds/methods by reference to a result to be achieved and a meaningful comparison with the prior art is impossible. Thus, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds as defined in claim 2. No opinion can be given on claim 1 and the related parts of the other claims

III-2. Claim 10 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

V-1. State of the art:

The following documents have been cited:

D1: CANDELORE MARI RIOS ET AL: "Phytosphingosine 1-phosphate: A high affinity ligand for the S1P4/Edg-6 receptor" BIOCHEMICAL AND BIOPHYSICAL

- RESEARCH COMMUNICATIONS, vol. 297, no. 3, 27 September 2002 (2002-09-27), pages 600-606, XP002324759 ISSN: 0006-291X
- D2: WO 03/062252 A (MERCK & CO., INC; BUGIANESI, ROBERT, L; DOHERTY, GEORGE, A; GENTRY, AM) 31 July 2003 (2003-07-31)
- D3: BRASHEAR KAREN M ET AL: "Nonpeptide glycoprotein IIB/IIIA inhibitors: 18. Indole alpha-sulfonamide acids are potent inhibitors of platelet aggregation" BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 7, no. 21, 4 November 1997 (1997-11-04), pages 2793-2798, XP004136532 ISSN: 0960-894X
- D4: TAKUWA Y ET AL: "The Edg family G protein-coupled receptors for lysophospholipids: their signaling properties and biological activities" JOURNAL OF BIOCHEMISTRY, JAPANESE BIOCHEMICAL SOCIETY, TOKYO, JP, vol. 131, no. 6, June 2002 (2002-06), pages 767-771, XP009028822 ISSN: 0021-924X

V-2. Novelty (Art. 33(2) PCT):

D1, D2 and D4 do not disclose indole derivatives. The indole derivatives of D3 lack the R1 substituent. Claims 2, 9 and the parts of claims 3-8, 10 which relate to these compounds are thus novel.

V-3. Inventive step (Art. 33(3) PCT):

D1 and D2 disclose S1P agonists, D1 in particular discloses compounds which have a high affinity for the S1P4-receptor. D1 is considered as representing the closest state of the art.

The problem to be solved by the present application is the provision of further S1P agonists, in particular selective S1P4-agonists. This problem has been solved (cf. test data in the description). Since neither of D1, D2 or D4 disclose indole derivatives as possible S1P agonists, the skilled man could not have predicted that the compounds according to claim 2 would have such activity. Claims 2, 9 and the parts of claims 3-8,

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10 which relate to these compounds fulfil thus Art. 33(3) PCT.